-- For example, Cystic fibrosis (CF), the most common inherited lethal disorder in Caucasian populations (~1 out of 2,500 life births), is characterized by bacterial colonization and chronic infections of the lungs. The most prominent bacterium in these infections is *P. aeruginosa*—by their mid-twenties, over 80% of people with CF have *P. aeruginosa* in their lungs (Govan, J. R. *et al.* (1996) *Microbiol Rev.* 60(3):539-74). Although these infections can be controlled for many years by antibiotics, ultimately they "progress to mucoidy," meaning that the *P. aeruginosa* forms a biofilm that is resistant to antibiotic treatment. At this point the prognosis is poor. The median survival age for people with CF is the late 20s, with *P. aeruginosa* being the leading cause of death (Govan, J. R. *et al.* (1996) *Microbiol Rev.* 60(3):539-74). According to the Cystic Fibrosis Foundation, treatment of CF cost more than $900 million in 1995.--

Please amend the paragraph beginning at page 4, line 22 as follows:

--Treatment of these so-called nosocomial infections is complicated by the fact that bacteria encountered in hospital settings are often resistant to many antibiotics. In June 1998, the National Nosocomial Infections Surveillance (NNIS) System reported increases in resistance of *P. aeruginosa* isolates from intensive care units of 89 % for quinolone resistance and 32 % for imipenem resistance compared to the years 1993-1997 (see the NNIS webiste). In fact, some strains of *P. aeruginosa* are resistant to over 100 antibiotics (Levy, S. (1998) *Scientific American.* March). There is a critical need to overcome the emergence of bacterial strains that are resistant to conventional antibiotics (Travis, J. (1994) *Science.* 264:360-362).--

Please amend the paragraph beginning at page 5, line 28 as follows:

-- In general, the invention pertains to the modulation of bacterial cell-to-cell signaling. The inhibition of quorum sensing signaling renders a bacterial population more susceptible to treatment, either directly through the host immune-response or in combination with traditional antibacterial agents and biocides. More particularly, the invention also pertains to a method for identifying modulators, *e.g.,* inhibitors of cell-to-cell signaling in bacteria, and in particular one particular human pathogen, *Pseudomonas aeruginosa*.--

Please amend the paragraph beginning at page 8, line 34 as follows:

-- In another embodiment, the invention is an isolated nucleic acid molecule comprising a polynucleotide that hybridizes under stringent conditions to a quorum sensing controlled genetic locus derived from the genome of *Pseudomonas aeruginosa*, wherein the genetic locus comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID

NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35 and SEQ ID NO:36, operatively linked to a reporter gene.--

Please amend the paragraph beginning at page 9, line 20 as follows:

--and detecting a change in the detectable signal to thereby identify the test compound as a modulator of quorum sensing signaling in bacteria.--

Please amend the paragraph beginning at page 10, line 13 as follows:

-- *Figure 1* depicts the paradigm for quorum sensing signaling in the target bacterium, *Pseudomonas aeruginosa*.--

Please amend the paragraph beginning at page 13, line 10 as follows:

--The invention is based on the interruption of bacterial cell-to-cell signaling, *i.e.*, quorum sensing signaling in order to render a bacterial population more susceptible to treatment, either through the host immune-response or in combination with traditional antibacterial agents and biocides. Thus, the invention provides a bacterial indicator strain that allows for a high throughput screening assay for identifying compounds that modulate, *e.g.*, inhibit bacterial cell-to-cell signaling. The compounds so identified will provide novel anti-pathogenics and anti-fouling agents.--

Please amend the paragraph beginning at page 13, line 21 as follows:

--The term "analog" as in "homoserine lactone analog" is intended to encompass compounds that are chemically and/or electronically similar but have different atoms, such as isosteres and isologs. An analog includes a compound with a structure similar to that of another compound but differing from it in respect to certain components or structural makeup. The term analog is also intended to encompass stereoisomers.--

Please amend the paragraph beginning at page 16, line 1 as follows:

-- Autoinducer synthase molecules can be obtained from naturally occurring sources, *e.g.*, by purifying cellular extracts, can be chemically synthesized or can be recombinantly produced. Recombinantly produced autoinducer synthase molecules can have the amino acid sequence of a naturally occurring form of the autoinducer synthase protein. They can also have a similar amino acid sequence which includes mutations such as substitutions and deletions (including

truncation) of a naturally occurring form of the protein. Autoinducer synthase molecules can also include molecules which are structurally similar to the structures of naturally occurring autoinducer synthase proteins, *e.g.*, biologically active variants.--

Please amend the paragraph beginning at page 17, line 1 as follows:

--The terms "derived from" or "derivative", as used interchangeably herein, are intended to mean that a sequence is identical to or modified from another sequence, *e.g.*, a naturally occurring sequence. Derivatives within the scope of the invention include polynucleotide derivatives. Polynucleotide or nucleic acid derivatives differ from the sequences described herein (*e.g.*, SEQ ID Nos.: 1-38) or known in nucleotide sequence. For example, a polynucleotide derivative may be characterized by one or more nucleotide substitutions, insertions, or deletions, as compared to a reference sequence. A nucleotide sequence comprising a quorum sensing controlled genetic locus that is derived from the genome of *P. aeruginosa*, *e.g.*, SEQ ID Nos.: 1-38, includes sequences that have been modified by various changes such as insertions, deletions and substitutions, and which retain the property of being regulated in response to a quorum sensing signaling event. Such sequences may comprise a quorum sensing controlled regulatory element and/or a quorum sensing controlled gene. The nucleotide sequence of the *P. aeruginosa* genome is available at the Pseudomonas Genome Project website.--

Please amend the paragraph beginning at page 21, line 24 as follows:

--As used interchangeably herein, the terms "transposon" and "transposable element" are intended to include a piece of DNA that can insert into and cut itself out of, genomic DNA of a particular host species. Transposons include mobile genetic elements (MGEs) containing insertion sequences and additional genetic sequences unrelated to insertion functions (for example, sequences encoding a reporter gene). Insertion sequence elements include sequences that are between 0.7 and 1.8 kb in size with termini approximately 10 to 40 base pairs in length with perfect or nearly perfect repeats. As used herein, a transposable element is operatively linked to the nucleotide sequence into which it is inserted. Transposable elements are well known in the art.--

Please amend the paragraph beginning at page 22, line 19 as follows:

-- Quorum sensing signal molecules that are useful in the methods of the present invention include autoinducer compounds such as homoserine lactones, and analogs thereof (see Table 1). In certain embodiments, the quorum sensing signal molecule is either 3-oxo-C12-homoserine lactone or C4-HSL. In one embodiment, the cell does not express the quorum sensing signal molecule. For example, the cell may comprise a mutant strain of *Pseudomonas*

aeruginosa wherein *lasI* and *rhlI* are inactivated. Therefore, the cell is contacted with an exogenous quorum sensing signal molecule, *e.g.*, a recombinant or synthetic molecule. In another embodiment, the quorum sensing signal molecule is produced by a second cell (*e.g.*, a prokaryotic or eukaryotic cell), which is co-incubated with the indicator cell. For example, an indicator cell which does not express a quorum sensing signal molecule can be co-incubated with a wild type strain of *Pseudomonas aeruginosa* which produces a quorum sensing signal molecule. Alternatively, the indicator strain which does not express a quorum sensing signal molecule is co-incubated with a second cell which has been transformed, or otherwise altered, such that it is able to express a quorum sensing signal molecule. In yet another embodiment, the quorum sensing signal molecule is expressed by the indicator strain.--

Please amend the paragraph beginning at page 26, line 4 as follows:

-- In one embodiment, the cell is contacted with an exogenous quorum sensing signal molecule, *e.g.*, a recombinant or synthetic molecule, as described herein. In another embodiment, the quorum sensing signal molecule is produced by a second cell (*e.g.*, a prokaryotic or eukaryotic cell), which is co-incubated with the indicator cell. For example, an indicator cell which does not express a quorum sensing signal molecule can be co-incubated with a wild type strain of *Pseudomonas aeruginosa* which produces a quorum sensing signal molecule. Alternatively, the indicator strain which does not express a quorum sensing signal molecule is co-incubated with a second cell which has been transformed, or otherwise altered, such that it is able to express a quorum sensing signal molecule. In yet another embodiment, the quorum sensing signal molecule is expressed by the indicator strain.--

Please amend the paragraph beginning at page 26, line 15 as follows:

-- Another aspect of the invention provides a mutant strain of *Pseudomonas aeruginosa* comprising a promoterless reporter gene inserted in a chromosome at a genetic locus comprising a nucleotide sequence set forth as SEQ ID NOs:1-36, *e.g.*, a quorum sensing controlled genetic locus. In one embodiment the reporter gene is contained in a transposable element. In another embodiment, the reporter gene is lacZ or GFP, or a variant thereof, *e.g.*, GFPmut2. In yet another embodiment, *lasI* and *rhlI* are inactivated in the mutant strain of *P. aeruginosa*. The above-described cells are useful in the methods of the instant invention, as the cells are responsive to a quorum sensing signal molecule such that a detectable signal is generated by the reporter gene. These cells are also useful for studying the function of polypeptides encoded by the quorum sensing controlled loci comprising the nucleotide sequences set forth as SEQ ID NOs.:1-36.--

Please amend the paragraph beginning at page 26, line 27 as follows:

-- Yet another aspect of the invention provides isolated nucleic acid molecules comprising a nucleotide sequence comprising a quorum sensing controlled genetic locus derived from the genome of *Pseudomonas aeruginosa* operatively linked to a reporter gene. In one embodiment, a reporter gene is operatively linked to a regulatory sequence derived from the genome of *P. aeruginosa*, wherein the regulatory sequence regulates a quorum sensing controlled genetic locus comprising a nucleotide sequence set forth as SEQ ID NO:1-36. In a preferred embodiment such regulatory sequences comprise at least one binding site for a quorum sensing controlled transcriptional regulatory factor (*e.g.*, a transcriptional activator or repressor molecule) such that transcription of the reporter gene is responsive to a quorum sensing signal molecule and/or a modulator of quorum sensing signaling. In another embodiment, a reporter gene is operatively linked to a quorum sensing controlled genetic locus derived from the genome of *P. aeruginosa*, wherein the genetic locus comprises a nucleotide sequence set forth as SEQ ID NO:1-36. In yet another embodiment, a reporter gene is operatively linked to a nucleotide sequence which has at least 80%, and more preferably at least 85%, 90% or 95% identity to quorum sensing controlled genetic locus derived from the genome of *P. aeruginosa*, wherein the genetic locus comprises a nucleotide sequence set forth as SEQ ID NO:1-36. In a further embodiment, a reporter gene is operatively linked to a nucleotide sequence which hybridizes under stringent conditions to quorum sensing controlled genetic locus derived from the genome of *P. aeruginosa*, wherein the genetic locus comprises a nucleotide sequence set forth as SEQ ID NO:1-36.--

Please amend the paragraph beginning at page 27, line 10 as follows:

-- The term "isolated nucleic acid molecule" includes nucleic acid molecules which are separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. For example, with regard to genomic DNA, the term "isolated" includes nucleic acid molecules which are separated from the chromosome with which the genomic DNA is naturally associated. Preferably, an "isolated" nucleic acid is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated nucleic acid molecule can contain less than about 5 kb, 4kb, 3kb, 2kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized. As used interchangeably

herein, the terms "nucleic acid molecule" and "polynucleotide" are intended to include DNA molecules (*e.g.*, cDNA or genomic DNA) and RNA molecules (*e.g.*, mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA. The term "DNA" refers to deoxyribonucleic acid whether single- or double-stranded. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules which include an open reading frame encoding a protein, preferably a quorum sensing controlled protein, and can further include non-coding regulatory sequences, and introns.--

Please amend the paragraph beginning at page 27, line 33 as follows:

--The present invention includes polynucleotides capable of hybridizing under stringent conditions, preferably highly stringent conditions, to the polynucleotides described herein (*e.g.*, a quorum sensing controlled genetic locus, *e.g.*, SEQ ID NOs.:1-36). As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences that are significantly identical or homologous to each other remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 80%, even more preferably at least about 85% or 90% identical to each other remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, Ausubel *et al.*, eds., John Wiley & Sons, Inc. (1995), sections 2, 4, and 6. Additional stringent conditions can be found in *Molecular Cloning: A Laboratory Manual*, Sambrook *et al.*, Cold Spring Harbor Press, Cold Spring Harbor, NY (1989), chapters 7, 9, and 11. A preferred, non-limiting example of stringent hybridization conditions includes hybridization in 4X sodium chloride/sodium citrate (SSC), at about 65-70°C (or alternatively hybridization in 4X SSC plus 50% formamide at about 42-50°C) followed by one or more washes in 1X SSC, at about 65-70° C. A preferred, non-limiting example of highly stringent hybridization conditions includes hybridization in 1X SSC, at about 65-70°C (or alternatively hybridization in 1X SSC plus 50% formamide at about 42-50°C) followed by one or more washes in 0.3X SSC, at about 65-70°C. A preferred, non-limiting example of reduced stringency hybridization conditions includes hybridization in 4X SSC, at about 50-60°C (or alternatively hybridization in 6X SSC plus 50% formamide at about 40-45°C) followed by one or more washes in 2X SSC, at about 50-60°C. Ranges intermediate to the above-recited values, *e.g.*, at 65-70°C or at 42-50°C are also intended to be encompassed by the present invention. SSPE (1xSSPE is 0.15M NaCl, 10mM NaH_2PO_4, and 1.25mM EDTA, pH 7.4) can be substituted for SSC (1X SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes each after hybridization is complete. The hybridization temperature for hybrids anticipated to be less

than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m(°C) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m(°C) = 81.5 + 16.6($\log_{10}$[Na^+]) + 0.41(%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na^+] is the concentration of sodium ions in the hybridization buffer ([Na^+] for 1X SSC = 0.165 M). It will also be recognized by the skilled practitioner that additional reagents may be added to hybridization and/or wash buffers to decrease non-specific hybridization of nucleic acid molecules to membranes, for example, nitrocellulose or nylon membranes, including but not limited to blocking agents (*e.g.*, BSA or salmon or herring sperm carrier DNA), detergents (*e.g.*, SDS), chelating agents (*e.g.*, EDTA), Ficoll, PVP and the like. When using nylon membranes, in particular, an additional preferred, non-limiting example of stringent hybridization conditions is hybridization in 0.25-0.5M NaH_2PO_4, 7% SDS at about 65°C, followed by one or more washes at 0.02M NaH_2PO_4, 1% SDS at 65°C (see *e.g.*, Church and Gilbert (1984) *Proc. Natl. Acad. Sci. USA* 81:1991-1995), or alternatively 0.2X SSC, 1% SDS.--

Please amend the paragraph beginning at page 29, line 3 as follows:

-- The invention further encompasses nucleic acid molecules that differ from the quorum sensing controlled genetic loci described herein, *e.g.*, the nucleotide sequences shown in SEQ ID NO:1-36. Accordingly, the invention also includes variants, *e.g.*, allelic variants, of the disclosed polynucleotides or proteins; that is naturally occuring and non-naturally occurring alternative forms of the isolated polynucleotide which may also encode proteins which are identical, homologous or related to that encoded by the polynucleotides of the invention.--

Please amend the paragraph beginning at page 29, line 36 as follows:

--The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP™ program in the GCG™ software package (available at the ACCELRYS™ website), using either a Blossom 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP™ program in the GCG™ software package (available at the ACCELRYS™ website), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. In another embodiment, the percent identity between two amino acid or nucleotide sequences is

determined using the algorithm of E. Meyers and W. Miller (*Comput. Appl. Biosci.*, 4:11-17 (1988) which has been incorporated into the ALIGN™ program (version 2.0) (available at the ALIGN™ website), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4.--

Please amend the paragraph beginning at page 30, line 14 as follows:

-- The nucleic acid and protein sequences of the present invention can further be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST™ and XBLAST™ programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST™ nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to nucleic acid molecules of the invention. BLAST™ protein searches can be performed with the XBLAST™ program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST™ can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST™ and Gapped BLAST™ programs, the default parameters of the respective programs (*e.g.*, XBLAST™ and NBLAST™) can be used. See the National Center for Biotechnology website. Additionally, the "Clustal" method (Higgins and Sharp, Gene, 73:237-44, 1988) and "Megalign" program (Clewley and Arnold, *Methods Mol. Biol*, 70:119-29, 1997) can be used to align sequences and determine similarity, identity, or homology.--

Please amend the paragraph beginning at page 32, line 18 as follows:

-- As used interchangeably herein, a "cell" or a "host cell" includes any cultivatable cell that can be modified by the introduction of heterologous DNA. As used herein, "heterologous DNA", a "heterologous gene" or "heterologous polynucleotide sequence" is defined in relation to the cell or organism harboring such a nucleic acid or gene. A heterologous DNA sequence includes a sequence that is not naturally found in the host cell or organism, *e.g.*, a sequence which is native to a cell type or species of organism other than the host cell or organism. Heterologous DNA also includes mutated endogenous genetic sequences, for example, as such sequences are not naturally found in the host cell or organism. Preferably, a host cell is one in which a quorum sensing signal molecule, *e.g*, an autoinducer molecule, initiates a quorum sensing signaling response which includes the regulation of target quorum sensing controlled genetic sequences . The choice of an appropriate host cell will also be influenced by the choice of detection signal. For example, reporter constructs, as described herein, can provide a selectable or screenable trait upon activation or inhibition of gene transcription in response to a

Q21 quorum sensing signaling event; in order to achieve optimal selection or screening, the host cell phenotype will be considered.--

Please amend the paragraph beginning at page 35, line 37 as follows:

--3.1-kb *P. aeruginosa* PAO1 chromosomal DNA fragment containing the *lasB* gene was amplified by PCR using the EXPAND™ Long Template PCR System (Boehringer Mannheim). This fragment was cloned into *Bam*HI-digested pSUP102. The resulting plasmid, pSUP102-lasB was digested with *Not*I, polished with T4 polymerase and ligated with the 6.5-kb *lacZ-aacC1* fragment from pTL61T-GMΩ1 to generate pMW300. The promoterless *lacZ* gene in pMW300 is 549 nucleotides form the start of the *lasB* ORF, it is flanked by 1.5 kb upstream and 1.6 kb downstream *P. aeruginosa* DNA, and it contains the p15A *ori,* which does not support replication in *P. aeruginosa*.--

Q22

Please amend the paragraph beginning at page 36, line 26 as follows:

--**Southern Blotting.** Chromosomal DNA was prepared using the QIAMP™ tissue kit (Qiagen Inc.). Approximately 2 μg of chromosomal DNA was digested with restriction endonucleases, separated on a 0.7% agarose gel, and transferred to a nylon membrane according to standard methods (Ausubel, F. *et al.* (1997) *Short Protocols in Molecular Biology.* (John Wiley & Sons, Inc., New York, N.Y.). DNA probes were generated using digoxigenin-11-dUTP by random primed DNA labeling or PCR. The Southern blots were visualized using the GENIUS™ system as outlined by the manufacturer (Boehringer Mannheim).--

Q23

Please amend the paragraph beginning at page 38, line 4 as follows:

--DNA sequences flanking Tn5-B22 insertions were located on the *P. aeruginosa* PAO1 chromosome by searching the chromosomal database at the *P. aeruginosa* Genome Project web site. The ORFs containing the insertions are those described at the web site. Functional coupling from the Argonne National Labs WIT website, sequence analysis, and expression patterns of the qsc mutants were used to identify potential operons (Overbeek, R. *et al.* (1999) *PNAS* 96, 2896-2901).--

Q24

Please amend the paragraph beginning at page 38, line 13 as follows:

--**Identification of *Pseudomonas aeruginosa* qsc Genes**. Seven thousand Tn5::B22 mutants of *P. aeruginosa* PAO-MW1 were screened. Tn5::B22 contains a promoterless *lacZ*. *P. aeruginosa* PAO-MW1 is a *lasI, rhlI* mutant that does not make acyl-HSL signals. Thus, transcription of the Tn5::B22 *lacZ* in a qsc gene was expected to respond to an acyl-HSL signal. The screen involved growth of each mutant in a complex medium in a microtiter dish well with

Q25

no added acyl-HSL, $3OC_{12}$-HSL, C_4-HSL, or both $3OC_{12}$-HSL and C_4-HSL. After 12-16 hours, β-galactosidase activity in each culture was measured. Two hundred-seventy mutants showed greater than 2 fold stimulation of β-galactosidase activity in response to either or both acyl-HSL. Of these, 70 showed a greater than 5-fold stimulation of β-galactosidase activity in response to either or both acyl-HSL, and were studied further. Each mutant was grown with shaking in culture tubes and 47 showed a reproducible greater than 5-fold stimulation of β-galactosidase activity in response to either or both of the acyl-HSL signals. These were considered to have Tn5::B22 insertions in qsc genes. It was shown by a Southern blot analysis with a *lacZ* probe that each mutant contained a single Tn5::B22 insertion.--

Please amend the paragraph beginning at page 39, line 26 as follows:

--Identity and Analysis of qsc Genes. The Tn5-B22-marked qsc genes were identified by coupling arbitrary PCR or transposon cloning with DNA sequencing. The sequences were located in the *P. aeruginosa* PAO1 chromosome by searching the *Pseudomonas aeruginosa* Genome Project web site (the Pseudomonas Genome Project website). To confirm the locations of the Tn5-B22 insertions in each qsc mutant, a Southern blot analysis was performed with Tn5-B22 as a probe. The sizes of Tn5-B22 restriction fragments were in agreement with those predicted based on the *P. aeruginosa* genomic DNA sequence (data not shown). The 47 qsc mutations mapped in or adjacent to 39 different open reading frames (ORFs). For example Figure 3 depicts the nucleic acid sequence of the quorum sensing controlled locus on the *P. aeruginosa* chromosome mapped in the *P. aeruginosa* mutant strain qsc102.--

In the Claims:

Please cancel claims 2 and 27-74, without prejudice, and amend claims 1, 3, 4, 7, 9, 17, 21, 24, 25, and 26 as follows:

1. **(Amended)** A method for identifying a modulator of quorum sensing signaling in bacteria, said method comprising:

providing a cell which is capable of endogenously synthesizing a quorum sensing signal molecule, wherein said cell comprises a regulatory sequence of a quorum sensing controlled gene operatively linked to a gene that generates a detectable signal in response to the quorum sensing signal molecule;

contacting said cell with a test compound;